

## SCIENTIFIC SECTION

### RABIES (HYDROPHOBIA).\*

BY E. G. STEWART, M.D.

Rabies, hydrophobia, canine madness or lyssa, is a highly infectious or communicable, rapidly fatal disease affecting practically all warm-blooded animals, especially those most commonly exposed to the bites of dogs, cats, coyotes, wolves and skunks affected with the malady. The Latin "rabies" is the best general term for the disease, in both man and animals.

Its communication from subject to subject depends upon actual inoculation, the virus or infective material being injected into the body organism through a wound made by the teeth or claws of the infected animal, chiefly the canine. Less frequently, fresh wounds, abrasions or even closely shaven surfaces which have come in contact with virulent saliva, may be the avenue of infection. Still another source of contamination is through autopsy wounds. Schroeder reported a few years ago two cases of deaths from rabies, one that of a coachman who was infected by the caresses on his face of his pet dog, that a few days later developed rabies, and the other, of a child that showed no signs of having been bitten.

As a disease entity, rabies is distinguished by its variable incubation period, one to ten months; the localization of the virus principally in the central nervous system and salivary glands with the ultimate destruction of the functioning power of the former and marked disturbance of the psychical faculties; by the short course of the developed disease and its uniformly fatal ending; by the protection afforded by inoculation with attenuated rabies virus, and by the great diversity of opinions which are still held in regard to its existence or non-existence.

There are still some individuals, including physicians, who are skeptical regarding, or even deny the existence of, rabies as a distinct disease; or, if recognizing it, they believe that the individual or animal bitten by an animal in perfect health is liable to become affected with rabies, should the offending animal develop the disease at any subsequent period, no matter how remote. To deliberately deny the existence of rabies, shows either a lack of information or is an impeachment of the sincerity and truthfulness of the men who have devoted years of disinterested study to the subject and who have presented to the scientific world, facts of observations and investigations which have proved rabies as much of a disease entity as scarlet fever, bubonic plague or smallpox. The multiplication of the living virus in the body, the communication and its mode of transmission by the affected animal to another perfectly healthy one, the multiplication of the virus and subsequent manifestation of symptoms of the disease in the second animal are procedures which have been demonstrated beyond a doubt. Every case of rabies presupposes a previous case of the disease. As to the query of the skeptic, relative to the origin of the first case, there is no answer, a mystery common to every animal and plant in the whole universe of living things, from the highest mammal to the most insignificant protozoa, from the mammoth trees to the micro-

---

\* Read before Scientific Section, A. Ph. A., Indianapolis meeting, 1918.

organisms. "To deny the existence of rabies because we cannot trace the virus to its primary origin is to use an argument that can be applied with equal justice to show the non-existence of both dog and master and everything else living and dead. Primary, fundamental or final causes are beyond human comprehension, and those persons who require them as a basis of their beliefs, if they are consistent, must necessarily deny the existence of everything."

While rabies is not to be compared with many other infectious diseases relative to its mortality rate among human beings, it does have a definite claim for attention at the present time. It annually claims a number of victims, for, as some one has said, this "madness" is not a lunacy with life but a sanity with inevitable death; it entails untold anguish and agonies of apprehension in exposed persons and in those who have had loved ones exposed; it causes each year no inconsiderable loss economically from the death of valuable stock. And all because we refuse to make use of the comparatively simple measures which would reduce the disease to a minimum or entirely eradicate it—the enactment of proper dog laws and the muzzling of all dogs. Since the introduction of such measures the disease has been diminished in most of the German states, and the cases reported have usually come from near the border line where muzzling is not enforced. With such laws, Denmark, Sweden and Norway have not known rabies for years and it has recently been eradicated from England and Switzerland. It has never been known in Australia, probably owing to the fact that a strict enforcement of a six months' quarantine for dogs is observed.

Of all the domestic animals, the dog and cat are given the most liberty. The dog is a social animal and the cat a solitary one; domestication and association with man have not changed their inherent qualities or traits. Therefore, in the transmission of rabies, the dog is the more dangerous of the two. But when it is suggested that this roaming at large be stopped and that the dog be muzzled, a great hue and cry goes up from so-called "dog lovers," yet in reality it is no more cruel to place a muzzle on a dog than it is to put a bit in the mouth of a horse, harness him with stiff, chafing leather straps and force him to draw loaded wagons. And, in the true evaluation of things, to be a friend of man is better than to be a friend of animals, for all the discomfort of all the muzzled dogs in the world is as nothing compared to the slightest anxiety and suffering of one human being from just the fear of rabies. One must needs wonder how long public sentiment is to remain out of focus on this subject, and defeat the efforts of organized medical bodies for the prevention of disease.

Therefore, in view of existing conditions, it is well for the physician and the pharmacist and even the laity to have the salient facts of rabies in mind, because the necessity for dealing with them usually comes without much warning except in recognized epidemics of the disease, and the problems relating thereto must be met promptly.

#### HISTORICAL.

The earliest record of rabies is said to be found in the writings of Aristotle:

"Dogs suffer from a madness which puts them in a state of fury and all animals which they bite in this condition become also attacked by madness."

We find mention of rabies in the works of Virgil, Horace, Ovid and Plutarch. No mention of human rabies is made until the first century A. D. when Celsus described it. In the second

century, Aurelianus recorded a definite description of the disease in man practically as we know it to-day. Nothing of the disease is recorded during the middle ages. In 1591, Bauhin speaks of the infection of human beings by rabid wolves. There was an epizootic of rabies in 1604 in Paris; toward the end of the seventeenth century in Italy; in 1708 in Suabia; in 1719-23 in France and Germany; in 1754-1760 in England; in 1779-1807 in America, especially in the West Indian Islands and Peru. In 1779 there was an epidemic in Philadelphia, and in 1873 one in New York and other parts of the United States. Toward the end of the eighteenth century and the beginning of the nineteenth century rabies had spread all over Europe. Attempts have been made in the past to secure data concerning its prevalence in the United States, and the positive results at hand indicate that nearly every state in the Union has at one time or other harbored this disease in man or animals. In the Western States, the infection is frequently found in skunks or coyotes.

The early conception of the disease was held until the nineteenth century when inoculation experiments and scientific investigation revealed its true infectious character. Some of these early beliefs were naturally the results of unscientific investigation and observation, but they are worthy of consideration and repetition because they are accurate, namely, that long-haired dogs are attacked less frequently than short-haired ones, an observation explained by the fact that the infected saliva is mechanically removed by the hair; the young dogs are more susceptible; that the saliva of dogs may be virulent before symptoms have appeared; that the fear of water is seldom observed in rabid animals, the so-called "hydrophobia" being due to an intense spasm of the muscles of deglutition which interferes with the animal's satisfying his thirst. In China no corresponding word for hydrophobia is known. Mad dogs may be playful at first, they do not necessarily froth at the mouth, appear wild or carry the tail between the legs.

Various erroneous and peculiar aetiological factors were designated to account for the disease, due to the very crude methods of diagnosis and to the fact that the disease was confused with other nervous conditions, and that, because of its long incubation period, its presence in man was not associated with previous injury received from a rabid animal. It was said to be produced by "evil spirits" and to be cured by pilgrimages. Fright produced it. The disturbed relations of body gases resulting in a poisoning of the blood is another cause given. Among the Chinese, the idea is still prevalent that dogs become mad from eating toads in the spring or breathing at snake holes the poisonous vapors given off by the hibernating snakes. Frederick the Great issued an edict that the "mad worm," supposed to be the cause of rabies, but since found to be a normal cartilage of the tongue, should be removed from all dogs. Deprivation of water, extremes of temperatures, especially heat, eating putrified materials or drinking foul water, lack of a meat diet in animals accustomed to meat have all been popular beliefs. A number of years ago, the president of a S. P. C. A. of one of our large cities said that if dogs were given all the water they needed to drink, there would be no such thing as rabies.

The remedies suggested for the prevention or cure of rabies are equally interesting. In China, a dose made by pulverizing certain small insects like lice, is considered a specific emulsion. May worms given in honey is an old-time remedy. Pliny the Elder recommended the livers of mad dogs as a cure for hydrophobia. By some, it was believed that the little figures of dogs, in reality blood clots, passed in the urine of a patient after the administration of cantharides were the cause of the disease and that their elimination in this manner would result in a cure. The "mad stone" as a curative agent is still devoutly believed in by a great many people in different sections of the country. A physician from one of our Southern States reported in a medical meeting last year the occurrence of three cases of possible exposure to a rabies infection; one of these was given the Pasteur treatment, one had the wound cauterized and the third had the mad stone applied. He apparently did not doubt the efficacy of any of the treatments. Some of these mad stones, properly called hair balls, are obtained from the stomachs of various wild and domestic animals. They are in some cases composed of matted hair which the animal has licked from its body and swallowed; but in the majority of cases they consist of masses of vegetable fiber which have gradually collected over a considerable period of time and formed into a spherical mass by the contraction of the gastric walls. After a person has been bitten, the mad stone is applied to the wound; if it adheres (which depends entirely upon the amount of hemorrhage) it will remove the poison, which can be detected by the discoloration produced when the stone is subsequently boiled in milk. Instances have been known where persons have made long journeys and paid large sums of money to have the mad stone applied. Celsus advised treating the bites

inflicted by dogs by suction and cauterization with the actual cautery. When the disease had developed, he recommended immersing the patient in cold water. This method of treatment persisted until the eighteenth century.

As a means of diagnosis, the bared breast of a living fowl was applied to the wound, if the fowl died it proved that the rabies poison was present, but if it lived, there was no danger to the bitten person. Another diagnostic method was to feed the exposed person some yellow or black beans. If the man found the taste pleasant and sweet and enjoyed them, he was mad, but if the taste was unpleasant, the poison of madness was not present.

In 1804 it was demonstrated by inoculation experiments by Zinke and Grüner and by Count de Salm-Reifersheid in 1813, that the saliva of a rabid dog was infective. In 1854, Virchow showed the fallacy of the spontaneous origin of the disease, and Galtier established the method of transmitting the disease to rabbits by subdural inoculation of the suspicious nerve substance. The researches of Pasteur and his co-workers demonstrated the location of the virus in its purest form in the central nervous system and gave the world protective inoculation or preventive vaccination.

Observations suggested and experiments proved that rabies was an infectious disease with symptoms referable to the nervous system, the propagation medium being the torn nerve fibers or nerve filaments at the site of the wound. The blood and lymph streams do not contain the causative agent or at least only rarely and are not usually regarded as sources of infection, but it is present in the salivary glands. Poor and Steinhardt isolated it from the salivary glands in 75 percent of all cases tested. The salivary glands in man rarely contain the microorganism. The mammary glands are occasionally invaded by the virus and milk may be a source of infection to the milker if he should happen to have cuts or bruises on his hands. Bordach records a case of a woman suffering from hydrophobia whose milk was demonstrated to contain the virus by inoculation into animals. A child she was nursing did not, however, contract the disease. Ingestion of the milk would not appear then to be a means of infection if the mucous membranes are intact, although rabbits have been inoculated successfully through the uninjured mucous membrane and one case of rabies in a nursing child has been recorded in the literature. The cerebro-spinal fluid is not infective. The skin may contain the virus at the point of inoculation, a fact which serves to emphasize the necessity of proper cauterization of the wound.

The nerve tissue of the body constitutes a perfect culture medium for the growth of the rabies microorganism, but the question of a successful artificial culture medium outside the body has not yet been settled. Noguchi reported the isolation of the rabies organism a few years ago. He states that he found, in a specially prepared culture medium, very minute granular and somewhat coarse pleomorphic chromatoid bodies which, on subsequent transplantations, reappear through many generations. By inoculating animals with cultures containing these bodies, rabies was produced in dogs, rabbits and guinea pigs as shown by the typical symptoms and further animal inoculations. His work has not as yet been confirmed by other observers. Remlinger, Poor and Steinhardt and others have demonstrated the filterability of the rabic virus. In 1903, Negri of the University of Pavia, Italy, described certain bodies which constantly occurred in certain nerve cells in cases of rabies. The relations of these bodies to the disease have been repeatedly confirmed and the demonstration of their presence in the cells of the

*cornu ammonis* is considered pathognomonic of the disease. Negri concluded from his studies that these bodies were probably protozoan in nature and the true causative agent. Other observers share Negri's belief, while still others are inclined to believe that they are merely cell reactions to the rabies virus. Since the discovery of the Negri bodies, it has been possible to make a laboratory diagnosis of rabies within a few hours. They are found in 96 to 98 percent of all cases of rabies that have been examined microscopically and are so permanent that their presence can be demonstrated some time after decomposition of the tissues has begun. The practical importance of their discovery apart from any ætiological relation which they may bear to the disease is obvious.

Rabies is commonly met with in mammals which are subjected oftenest to the bites of dogs, wolves, etc., but all warm-blooded animals are susceptible. The dog is most frequently affected. In Russia and in other limited areas, the wolf stands next. Cattle are often attacked by wandering rabid dogs. Cats are frequently infected, oftener than is usually suspected, because they develop the dumb form of rabies which means that no diagnosis, except of sickness, is made. Cases of human rabies are not so frequent as formerly because of the wide application of the preventive treatment.

Dogs, whether mad or not, are more active in biting during the summer months. The reason for this may be that especially during that time of the year, many street animals suffer from heat and thirst and the deprivation makes them irritable or they may be subjected to an unusual amount of teasing. These are the months, too, when people are much in the open. This is particularly true of children during the vacation months. Their chances of exposure to bites of animals are increased many-fold. One writer states that the number of applicants for treatment at a Pasteur Institute in the Northwest during the summer months far exceeds the number of persons who apply for treatment during the winter months, but that it is necessary to treat only 25 percent of such applicants since negative results for Negri bodies occur in 75 percent of animal brains examined, while in the winter, it is necessary to treat 60 percent of all applicants. In large cities, the cases of rabies in the dog are more frequent in winter than during the summer months. The idea is prevalent that animals are particularly liable to go mad during the so-called "dog days" which extend from the first of July to the middle of August. The reason these days were so designated was because they covered a period when the dog star, Sirius, was above the horizon. They have no connection or association with the dog or the presence of rabies.

The proportion of persons who, after being bitten, will develop rabies has been variously estimated. Tardieu and Bouley in France collected 855 cases, of which 399 or 46.6 percent died. According to the report of the Pasteur Institute of Kasauli, India, in 1908, 35 percent of untreated cases developed rabies. The statistics of Doebert show a mortality of 14.8 percent in 122 untreated cases; Horsley gives 16 percent; Reifer 15 percent and Högyes 15 to 16.5 percent. In the United States, there are no available statistics; Brawner followed in the newspapers such cases of bites and deaths as were reported to have occurred within the Southern States, and of 80 persons untreated except for the mad stone, there were 16 deaths reported, 20 percent. The ratio 1 to 6 would probably approximate the truth.

RABIES TABLE PERCENTAGE MORTALITY.

Character and site of bite.	By wolf.	By cat.	By dog.
Multiple and deep wounds about eye, nose or lips.....	100	70	60
Multiple and deep wounds about other parts of face.....	80	50	50
Multiple and deep wounds on other parts of uncovered body.....	40	40	30
Single and deep wounds on finger or neck.....	20	20	15
Deep on well-covered parts of the body.....	15	10	3
Superficial on uncovered parts of the body.....	10	10	10
Same with hemorrhage.....	2	2	2
Contact of recent wounds with infected saliva.....	0.1	0.1	0.1
Contact of wounds more than 24 hours old.....	0	0	0

This gives a general average of 24 percent after dog bites.

Generally speaking, the more numerous and the deeper the wounds, the greater the danger of rabies developing. The mortality rate is higher when wounds are inflicted on bare parts, due to the fact that the saliva is wiped off when the bite is through clothing and not so much infective material enters the injured part. The nerve supply also determines susceptibility to the development of rabies. Face bites are the most dangerous. Statistics show that 90 percent of face bites are fatal. Bites on the finger tips are next in importance. The mortality from bites on the hands and wrists is 65 to 70 percent; on the arms, 30 to 35 percent; on the limbs (lower), 20 to 25 percent; and on the trunk, 5 to 10 percent.

The incubation period is variable, from ten days to many months. In human cases, the long incubation period enables the individual to avail himself of the prophylactic treatment. The length of the incubation is influenced by a number of factors, such as—the species of animal, the period being longer in man; the site of the injury, the virus travels by way of the nerve paths to the central nervous system and there is a shorter incubation period in cases where the injury sustained is near the brain or large nerve trunks, such as head and face bites; children and females have a shorter incubation, in the former this is probably due to the fact that most of the bites are about the face and hands; severity of wounds, lacerated wounds involving nerve trunks result in a shorter incubation period for they permit the introduction of a greater amount of infective material. The danger increases in direct proportion to the number of bites even though they may be slight; a weakened condition of the nervous system will determine a shorter incubation period, alcoholics and neurasthenics, syphilitics and those suffering from other nervous diseases will exhibit an earlier manifestation of the condition.

Friedberger and Frohner give the following figures for the incubation period in animals: ox, four to eight weeks; horse, four to eight weeks; cats, two to four weeks; sheep, three to four weeks; poultry, six weeks to eleven months. Bauer gives the following periods for human rabies: males, 80 days; females, 65 days; children, 57 days.

There are two clinical types of rabies in animals, the furious, due to excitation or irritation; and the dumb or paralytic, due to rapid degeneration. Many cases present a mixed type and a few are atypical. In the furious type, the most marked symptoms are the change in disposition, either in the direction of increased irritability and ugliness or unnatural playfulness and exhibition of affection; an increased hypersensibility to all external stimuli and the tendency to wander off, returning after several days, ill and emaciated and wounded from engagements

with other animals. He may have traveled a distance of from twenty to twenty-five miles. There is also a marked tendency to snap and bite, this being merely an expression of intense irritability. In some cases, he bites himself, usually at the point where he himself was bitten. The voice is changed, being hoarse and of lower pitch than usual. He does not eat the customary food but betrays an abnormal appetite for sticks, stones, etc. Swallowing becomes difficult and the irritability increases until the animal becomes furious and convulsions appear or paralysis supervenes. Death is caused by the ascent of the paralysis to the respiratory centers.

In the dumb form or the "black tongue," in the vernacular of the South, there is not the frank exhibition of rabies seen in the furious form, and for this reason, it is particularly dangerous to man. Often the most conspicuous symptom is the spasm of deglutition and the paralysis of the throat muscles giving the observer the impression that the animal has a bone in its throat, and often, the attempt on his part to relieve the animal results in exposure to the disease. The animal does not bite, but the saliva is virulent and may cause rabies if it comes in contact with recent wounds or abrasions of the skin. The animal will lie quietly in some secluded spot and appear stupid. The paralysis of the jaw is early, the tongue protrudes and becomes covered with dirt which gives rise to the expression "black tongue." Death usually occurs in about three days, whereas the furious type lasts from six to eight days; 15 to 20 percent of all cases of rabies in dogs are of the dumb type.

The premonitory symptoms of rabies in man resemble those of any infectious disease, irritability, anorexia, insomnia, depression and malaise and some stiffness of the neck and shoulder muscles. In some cases the first intimation the patient has that something is wrong is in the difficulty experienced in taking a drink. There is a constriction of the pharynx which though transitory reappears each time an attempt is made to drink. The healed wound sometimes becomes sensitive with tingling and itching or even pain. There is a moderate rise of temperature. The spasmodic stage is initiated after about twenty-four hours, and spasms result from the slightest stimuli. Mental excitement ensues and the furious stage supervenes within the next forty-eight hours or less with its maniacal delirium. The patient may die at this stage or pass into a paralytic stage in which the muscles relax, the jaw drops and the patient is comatose, the pulse irregular and the temperature high. Death occurs within five or six days and is inevitable. The delirium and mania, the violent spasms with inability to swallow are fearful to observe and physicians no matter how extensive their experience with human suffering find it difficult to erase the horror of these cases from their minds. In neurotic or debilitated subjects or in cases of multiple lacerations, the phenomena of infection are those of paralysis.

Lyssaphobia or fear of rabies is sometimes met with in neurotic individuals, but usually the symptoms, hysterical in character, come on within a few days after the assumed exposure. The occurrence of symptoms like those of rabies at a period less than two weeks after exposure should be regarded as suspicious. The first manifestation may be a hydrophobia, fear of water, and a good imitation of a dog's bark and to some extent its action, the patient going around on all fours and biting at the furniture. It is stated that hypersensitiveness to drafts of air,

which is very common and pronounced in true rabies, is not simulated in hysteria. This may be tested by stepping unobserved behind the patient and fanning him. A convulsive seizure would serve to support a diagnosis of real rabies. Usually other hysterical stigmata are present and the symptoms are amenable to treatment and the patient recovers.

Up to the present time, there has been no cure for rabies after the symptoms have once appeared. Almost every drug in the pharmacopoeia has been suggested as a possible remedy but the cures reported have never been scientifically proved. At present the developed disease must be treated symptomatically.

Preventive treatment consists, first, in the proper care of the wounds inflicted by the biting animal. Bleeding should be encouraged, as a free flow of blood will carry off some of the virus. After thorough cleansing of the wound, it should be cauterized. For this purpose, fuming nitric acid is to be preferred. Cabot in a series of experiments found that he could save 76 percent of animals when nitric acid was applied to wounds inflicted by rabid animals. Other agents used for this purpose are turpentine, hydrogen peroxide and tincture of iodine. The cautery should be applied early, not later than a half to one hour, in order for it to be effective, and it should be thoroughly applied, enlarging the wound if necessary, in order to reach the deeper parts of the wound, exercising, of course, due caution. But it must be remembered that no matter how carefully the local treatment is conducted, this does not obviate the necessity for constitutional treatment, which consists of the injection of a specific vaccine. Immunization with a living virus simulates most closely that produced in the body in overcoming an infection. In man, so far, only attenuated virus has been used. This manner of producing an artificial immunity was first demonstrated by Jenner in prophylaxis against smallpox. Pasteur recognized that Jennerization had other applications and similarly used an attenuated culture of rabies virus to establish protection against rabies.

His method was to modify "street virus" or the virus which occurs in nature, by passing it serially through monkeys and then to bring the virus up to a fixed degree of virulence by serial inoculations of rabbits giving the "fixed virus," a virus which produces the disease constantly within six to eight days after inoculation intracerebrally. Later in his work the first step was omitted and only the rabbits were used to modify and fix the virus. Proper attenuation of the spinal cords of animals dead from fixed virus inoculation was secured by drying them over potassium hydrate. The initial treatments were made with cords that had been drying a long time. Pasteur began with a fourteen-day cord and carried the treatment on for eighteen days, the later treatments being made from cords which had not been hanging over the potassium hydrate for so long a time. The Pasteur treatment depends on the fact that the spinal cord of a rabbit that has been inoculated with "fixed virus" and dead of rabies in six to eight days loses its virulence from day to day so that at the end of fourteen days it is entirely incapable of producing rabies when inoculated into a healthy animal. Beginning treatment with an emulsion of a small piece of cord that is not virulent or only slightly so, the patient is inoculated daily for eighteen to twenty-one days with varying strengths of the virus thus gradually establishing an immunity against the infec-

tion. There is involved the same principle familiar to us all in the establishment of drug toleration.

Thirty-five years ago, Pasteur established the first Pasteur Institute in Paris, and, in the July after its establishment, an Alsace child who had been severely bitten by a known mad dog was admitted for treatment. Pasteur and his associates believed that the child would die anyway and that the treatment which had been a success with animals should be given a trial at least. The inoculations were made for eighteen days and it is said that during that time, and for many weeks after, Pasteur lived in constant terror. On all sides he was severely criticized but he was confident and went ahead. The next patient treated was Julipe, a shepherd who is now a concierge at the Institute, a place which he has held practically since his treatment. The success of the method was soon assured and it was rapidly adopted in many countries, and Pasteur Institutes established. Pasteur Institutes are of two kinds, public and private. Public Pasteur Institutes are established by endowment, such as the Pasteur Institute in Paris, by governments such as those of the United States Public Health and Marine Service at Washington, the New York City Board of Health, Mexico City, and the various State Boards of Health, by universities and the Pasteur Institutes of the Universities of Moscow and Bucharest. Private Pasteur Institutes are what the name implies.

The value of the Pasteur antirabic treatment can not be overestimated. Official records have never been satisfactorily kept and mortality percentages differ but it is safe to estimate the mortality rate in untreated cases at 20 percent. The Institute in Paris was established in 1886. From that time until 1911, 32,397 patients had been treated with 128 deaths, a mortality rate of 0.39 percent. The first Pasteur Institute in the United States was opened in 1890. During the first eleven years, 1,608 persons were treated with a mortality rate of 0.68 percent. In general it may be said that the mortality of treated persons is about one percent, one-half of which could not, from the nature of their wounds, be immunized. The duration of the immunity induced by treatment is apparently variable. Experimental animals show a complete immunity even after eighteen months, but in humans there is no way of determining its duration, but it is probably much shorter than that in animals. Williams reports a case in which the immunity was less than fourteen months. Failure to establish an immunity may be due to the virulence of the infection, proximity of the wound to the nerve centers, or delay in the administration of antirabic treatment.

It is apparent that many animals (rabbits) must be sacrificed to prepare the rabies vaccine, but it is a sacrifice which is necessary to the conservation of human life and even the life of other animals. The words of Charles Eliot tersely state the creed of the scientist: "The humanity which would prevent human suffering is a deeper and truer humanity than the humanity which would save pain or death to animals."

The ill effects from the treatment are, as a rule, of minor importance. Usually during the second week of treatment there is some local reaction, such as slight swelling and tenderness at the sites of injection (the injections are made subcutaneously, the anterior wall of the abdomen by choice) lasting from twenty-four to seventy-two hours. The slight induration remaining, is absorbed slowly. Stim-

son regards this as a manifestation of hypersusceptibility to the foreign nerve tissue which is introduced.

Obese people show more local reaction than do thin people and children. In the latter, various skin rashes, which usually take the form of a mild urticaria (hives), have been observed.

The patient may complain of nervousness or sleeplessness, or, on the other hand, of drowsiness, for the first few days after institution of treatment. There is occasionally some headache or a feeling of malaise, or even slight affections of the nervous system, as restlessness, numbness and tingling of the extremities, but these are of short duration. Paralyzes have occurred very infrequently with some of the older modifications of the Pasteur method as well as with the classical Pasteur, cases having been reported from all except those modifications presented by Högyes and Harris. Various explanations have been offered for the occurrence of these paralyzes, but none of them is wholly satisfactory. The predisposing factors seem to be alcoholism, syphilis, and neurasthenia, according to some authorities. It must be understood that these cases of paralysis do not impair the value of the antirabic treatment any more than the deaths resulting occasionally from the administration of anesthetics, or from anaphylactic shock after the injection of diphtheria antitoxin, can be considered arguments against their use.

There are no contraindications to the institution of antirabic treatment. As stated, syphilitics, alcoholics and people affected with nervous disorders are more apt to exhibit hypersusceptibility to the injections. Pregnant women have taken the course without any disturbance, and Stimson reports a case of a boy with St. Vitus dance who seemed improved after the injections.

The brilliant results made possible by the Pasteur method have been the marvel of the scientific world and any modifications of the original method which have been devised from time to time are no criticism of the efficacy of the mother method; rather they have been efforts to so simplify the Pasteur technique that it might have a wider application. The Pasteur method requires a long time to complete the treatment and attendance at an institute necessitates considerable inconvenience and expense, and a large amount of laboratory equipment and animal material must be had for the maintenance of treatments.

There are many of these modifications. All make use of the fixed virus, but the method of cord attenuation varies for the purpose of preventing the loss of the immunizing properties, by the use of artificial gastric juice, phenol, mechanical disintegration and antirabic serum, which has been found capable of neutralizing fixed virus outside the body. Some make use of a dilution of the fresh material and all have for their ultimate purpose a shorter treatment period with a vaccine of increased antigenic (immunizing) power.

Among the best known modifications are the following:

1. The dilution of the fresh fixed virus (Högyes).
  2. Fixed virus attenuated by heat (Babes).
  3. Fixed virus attenuated by phenol (Fermi).
  4. A mixed treatment with specific serum and vaccine (Marie and Remlinger).
- Curative effects with antirabic serum (serum of sheep which have been immunized

against rabies infection) have not been satisfactorily established, but Babes claims that it is useful in combination with the vaccine, a mixture of the two being injected in severe cases.

Among the more recent methods devised and one which has attracted a good deal of attention because of its efficacy, safety, and standardization of dosage, which is not had in the classical method, is that of Harris, of St. Louis. Dr. Harris uses both the brains and cords of animals dead from fixed virus inoculation, grinds them to a paste, freezes and pulverizes and dries *in vacuo*. The resulting fine powder has practically the same infectivity as the fresh material and can be kept indefinitely provided it is properly protected from heat, light and moisture. It is a method which bids fair to still further reduce the small percentage of failures and to lessen the proportion of injurious or untoward results of treatment.

As to the indications for institution of antirabic treatment, a few brief statements may be made. The biting animal is the best witness for the patient and the diagnostician as well as for himself. In every accident, where there is a possibility of rabies infection involved, inquiry should be made as to the circumstances under which it occurred, the actions of the offending animal and the number of persons exposed to possible infection. While a biting dog may not always be a "mad dog," he is still a suspicious character, subject to arrest, but entitled to a trial by jury. The virus is present in the saliva several days before the onset of active symptoms (two to eight days), therefore, it is very unwise to permit the animal to escape or be killed as is so often done. The only exception to this general rule would be in the case of an animal already manifesting symptoms of rabies and so diagnosed by a veterinarian, or one which is "running mad."

Remlinger gives us the most helpful outline referring to indications for anti-rabic treatment.

If the biting animal	{	(1) Has died within 10 days after the biting	}	Anti-rabic
		(2) Has been killed within 10 days after the biting		Treatment
		(3) Has disappeared within 10 days after the biting		Indicated
		(4) Is unknown to the individual	}	Anti-rabic
		(A) Becomes ill with rabies		Treatment
(B) Dies with suspicious symptoms of rabies or another disease	Indicated			
(5) Has remained alive and under observation for ten days	}	No		
(D) Remains well both during and after the period		Treatment		

#### ABSTRACT OF DISCUSSION.

**THE CHAIRMAN:** This has been an extremely interesting paper. I believe it is the first time the subject of rabies has been presented in such a brilliant and popular form.

**J. N. HURTY:** I wish to make a personal acknowledgment of the excellent paper which has been read by Miss Stewart and to ask only one question. Why do you believe, Doctor, that we should take with some doubt the statement "that rabies will develop after ten or eleven months of incubation?" I happen to know an instance where it developed in eleven months without doubt. It seems to me there is no doubt that it will develop within that time, but why should you doubt it? We know that the infection of tuberculosis will lie in the body for years and years and finally develop. Why not so with rabies? I would just like to know why you said that. You seemed to be quite positive about it.

DR. E. G. STEWART: I understand there are only occasional cases. I did not mean to make it so positive that there would never be any, because there might be. I have a case that developed in six months, but such cases are very rare.

JACOB DINER: I am glad to have heard Dr. Stewart bring out the point of the sympathy for dogs and the lack of sympathy for human beings. Some cities are mightily interested in seeing that the poor dogs do not suffer, so they catch them by the hundred and asphyxiate them; but they do not permit the laboratories to obtain an animal for experimental purposes. In New York they have great difficulty in getting dogs for experimental purposes, and daily hundreds of dogs are asphyxiated by the Society for the Prevention of Cruelty to Animals.

BIOLOGICAL LABORATORIES,  
ELI LILLY & Co., INDIANAPOLIS, IND.

---

## VACCINE THERAPY IN THE LIGHT OF FACTS.\*

BY ALEXANDER M. ROVIN.

Skepticism gives no impetus to the progress of science. On the contrary, it has long been recognized as an element of retrogression.

The human race has fought disease always in a spirit of optimism. This made possible what has been accomplished in conquering epidemics. Brilliant, practical and scientific discoveries in Bacteriology and Pathology have given us aid long looked for to clear up many disputed opinions concerning the control and treatment of infectious diseases.

Since the dawn of man, the human race in its struggle has endeavored to overcome many forces in nature and become master of the earth.

Intelligence is the great force in developing and cultivating man's faculties, in his adaptation of nature's forces, in overcoming diseases. Notwithstanding the many misdirected efforts of our civilization, we have made sufficient strides in general knowledge to make bacteriology, the basic science of preventative medicine, possible. By applying the discoveries made in bacteriology, the burden of disease is lightened, sickness becomes less frequent and less prolonged, a greater degree of health is secured, the efficiency of the individual and the nation is increased and life is lengthened and made more enjoyable. The eradication of bacterial infections looks more hopeful than ever, since standard bacterial suspensions have been successfully applied in the prevention and treatment of bacterial diseases. Bacterial vaccines offer the necessary stimulus in raising body resistance, preparing—so to speak—body cells (immunizing mechanism) for the adequate production of antibodies that make germ life and its destructive invasion impossible.

Antibodies are regarded as cell secreted destructive ferments and there are at least several varieties of them, *i. e.*,

- (a) Bacteriocidins, which kill bacteria.
- (b) Bacteriolysins, which dissolve bacteria.
- (c) Agglutinins, which clump bacteria and render them inactive.
- (d) Opsonins, which prepare bacteria for ingestion and digestion

by leucocytes, or so to speak, prepare them for injection by fighting cells that ingest bacteria. If the leucocytes are successful in ingesting all the bacteria, they are victorious and their victory means the overcoming of the infection. If, on the contrary, the leucocytes retreat

---

\* Read before Scientific Section A. Ph. A., Indianapolis meeting, 1917.